

Complete Summary

GUIDELINE TITLE

Lymphogranuloma venereum (LGV). In: Sexually transmitted infections: UK national screening and testing guidelines.

BIBLIOGRAPHIC SOURCE(S)

Herring A, Richens J, LGV Incident Group, Health Protection Agency.
Lymphogranuloma venereum (LGV). In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 57-62. [17 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Lymphogranuloma venereum (LGV)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Urology

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide advice on what tests for lymphogranuloma venereum (LGV) are most appropriate in a United Kingdom (UK) genitourinary (GU) clinic setting (excluding human immunodeficiency virus [HIV]-infected patients)
- To provide a basis for audit
- To support clinics when bidding for additional resources to meet national standards

TARGET POPULATION

Patients in the United Kingdom presenting with suspected lymphogranuloma venereum (LGV)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Nucleic acid amplification test (NAAT) for detection of *Chlamydia trachomatis*-specific deoxyribonucleic acid (DNA)
2. Real-time polymerase chain reaction (PCR) for confirmation
3. Restriction endonuclease digestion
4. Restriction fragment length polymorphism (RFLP)
5. DNA sequencing of the *omp1* gene (only at a reference laboratory)
6. Specimen culture
7. Testing sites (ulcer, lymph node aspirate or biopsy, rectal swab or biopsy, urine, urethral swab, clotted blood)
8. Frequency of testing
9. Follow-up testing for cure
10. Screening of sexual contacts

MAJOR OUTCOMES CONSIDERED

Reliability of test methods (validity, sensitivity, specificity)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The main evidence for the development of this guideline was obtained by searching 'Medline' using the term 'lymphogranuloma venereum'. The Cochrane Library was also searched (no records). In addition, standard text books were consulted as was the 2002 Centers for Disease Control and Prevention (CDC) sexually transmitted infections (STI) treatment guidelines.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well designed quasi-experimental study

III: Evidence obtained from well designed non-experimental descriptive studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guidelines have been developed following the methodological framework of the Appraisal of Guidelines Research and Evaluation instrument (AGREE - adapted as described in *Int J STD and AIDS* 2004 15:297-305).

The extent to which the guideline represents the views of intended users has been addressed primarily by the authorship coming from the multidisciplinary membership of the Bacterial Special Interest Group (BSIG). As practising clinicians the authors were able to draw on their experience of applying the tests to symptomatic and asymptomatic patients but it was not feasible to obtain formal input from representative patients.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations

- A. Evidence at level Ia or Ib
- B. Evidence at level IIa, IIb, or III
- C. Evidence at level IV

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After drafting, other health care professionals and professional bodies in genitourinary (GU) medicine were asked to comment, the draft guidelines posted on the British Association for Sexual Health and HIV (BASHH) website for 3 months, and all comments reviewed before final publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the level of evidence (**I-IV**) and grade of recommendation (**A-C**) are provided at the end of the "Major Recommendations" field.

Widespread screening is currently not recommended; the need to test for lymphogranuloma venereum (LGV) will arise in the following patients:

- Patients presenting with an acute proctitis who have been at high risk.

- Patients presenting with inguinal buboes (inflammatory lymph node swellings in the inguinal-femoral lymph gland group), and a suggestive travel history.
- Patients with manifestations of late stage disease
- Sexual contacts of confirmed cases of LGV infection

Recommended Tests

The laboratory diagnosis is dependent on the detection of *Chlamydia trachomatis* (*C. trachomatis*) specific DNA followed by genotyping to identify serovars L1, L2 or L3.

- The method of choice for the laboratory diagnosis of LGV is the detection of *C. trachomatis* specific DNA belonging to an LGV serovar, L1, L2 or L3.
- The first step is the detection of *C. trachomatis* using a nucleic acid amplification test (NAAT). Routinely available NAATs for *C. trachomatis* will detect all serovars including LGV serovars and are licensed for genital specimens. However, rectal specimens need to be tested in most patients recently identified. There are no licensed NAATs for the detection of *C. trachomatis* in rectal specimens, but data is available supporting the validity of these tests for use with rectal specimens (**Evidence Level III, Grade of Recommendation B**).
- Confirmation of the presence of LGV specific deoxyribonucleic acid (DNA) can then be obtained by direct detection of LGV specific DNA using real-time polymerase chain reaction (PCR). Alternatively genotyping can be performed by amplifying the *omp1* gene followed by restriction endonuclease digestion to identify specific serovars. An additional restriction fragment length polymorphism (RFLP) method is based on the digest of the *CrP* gene which differentiates between L1-3. (**Evidence Level III, Grade of Recommendation B**).
- The Health Protection Agency has published an algorithm for the detection of LGV, which recommends that any NAAT positive for *C. trachomatis* from men who have sex with men presenting with proctitis should be sent to the Sexually Transmitted Bacteria Reference Laboratory (STBRL) for confirmation. At STBRL, the *C. trachomatis* status of the specimen will be confirmed using an 'in house' real-time PCR with independent primers specific to all unknown *C. trachomatis* strains. Specimens positive for *C. trachomatis* will be screened using reverse transcriptase (RT)-PCR to detect LGV serovars directly including L1, L2 and L3. Any LGV positive samples will be genotyped to determine the LGV serovar. (**Evidence Level III, Grade of Recommendation B**).
- Typing for epidemiological purposes using DNA sequencing of the *omp1* gene should only be performed at a reference laboratory.
- Culture is the most specific test but very few laboratories have culture facilities and sensitivity can be prejudiced by the toxic nature of bubo aspirates (**Evidence Level IV, Grade of Recommendation C**).
- Serology may be useful if direct detection has been unsuccessful. A high titre in a patient with symptoms is highly suggestive of LGV. However, a low titre cannot exclude LGV and a high titre in the absence of symptoms cannot confirm LGV. The two methods most used have been complement fixation (CF) and microimmunofluorescence-immunoglobulin G (MIF-IgG); single point titres of greater than or equal to 1/64 (**Evidence Level IV, Grade of Recommendation C**) and 1/256 respectively are considered positive. The

whole inclusion fluorescence test has also been used. Where MIF is used, it is important that a L serovar is included as an antigen.

- There are now many commercial immunoassays on the market for *C. trachomatis* serology but their use for LGV diagnosis has not been reported. Many of these kits use undisclosed peptide antigens that may not include LGV serovar sequences and thus are not recommended.

Recommended Sites for Testing

- Ulcer material (if ulcer is present)
- Lymph node aspirate (may require injection and re-aspiration of saline)
- Lymph node biopsy (if investigation by other means is unsuccessful)
- Rectal swabs (if proctitis is present)
- Urine
- Urethral swab
- Rectal biopsy tissue
- Clotted blood (for serology)

Factors Which Alter Tests Recommended or Sites Tested

Sites for testing will be determined by the clinical presentation. Clinicians should consult with their microbiology laboratory colleagues to alert them regarding unusual specimens and to inform them that specialist tests will be required.

Sexual History

- Travel to, and sexual exposure in, an LGV endemic country by the index patient or his/her partner (no alteration to standard recommendation).

Risk Groups

- Men Who Have Sex with Men (MSM) with high risk behaviour, in particular attendance at sex parties, anonymous sex, fisting and use of enemas (no alteration to standard recommendation).
- Patients who are known contacts of the infection (no alteration to standard recommendation)

Recommendation for Frequency of Repeat Testing in an Asymptomatic Patient

DNA Amplification Tests: Repeat testing four weeks after exposure only in individuals with known or strongly suspected exposure to LGV if the initial test has been done within three weeks of exposure and epidemiological treatment has been declined.

Serology: Repeat testing is only required if symptoms suggestive of LGV develop following the initial test.

Recommendation for Test of Cure and Follow Up

Test of cure is necessary and should be provided 3 to 5 weeks after treatment. For those very few patients who may have extensive lesions or fistulas as a result of late treatment, surgical intervention may be required.

Definitions:

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

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Grading of Recommendations

- A. Evidence at level Ia or Ib
- B. Evidence at level IIa, IIb, or III
- C. Evidence at level IV

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate screening of lymphogranuloma venereum (LGV) infection

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline recommends the use of deoxyribonucleic acid (DNA) amplification tests that may not be available in all microbiology laboratories.
- The identification of lymphogranuloma venereum (LGV) strain infection by *omp1* sequence analysis will incur additional costs for primers and sequencing reactions. It will also need to be performed by a Clinical/Biomedical Scientist skilled in polymerase chain reaction (PCR) and amplicon purification.
- The serological tests recommended are available only in a limited number of laboratories.
- The rare nature of this disease precluded patient consultation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Herring A, Richens J, LGV Incident Group, Health Protection Agency. Lymphogranuloma venereum (LGV). In: Ross J, Ison C, Carder C, Lewis D, Mercey D, Young H. Sexually transmitted infections: UK national screening and testing guidelines. London (UK): British Association for Sexual Health and HIV (BASHH); 2006 Aug. p. 57-62. [17 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Aug

GUIDELINE DEVELOPER(S)

British Association for Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

No specific or external funding was sought or provided in the development of this guideline.

GUIDELINE COMMITTEE

Screening Guidelines Steering Committee
Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Alan Herring, formerly Head of the PHLS Genitourinary Infections Reference Laboratory, Bristol; John Richens, Department of Sexually Transmitted Diseases, University College, London

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Conflict of interest: None

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from [British Association for Sexual Health and HIV Web Site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Specifications for the development of UK guidelines on the management of sexually transmitted infections (STIs) and closely related conditions 2005. London (UK): British Association of Sexual Health and HIV (BASHH); 2005. 14 p. Electronic copies: Available in Portable Document Format (PDF) from the [British Association for Sexual Health and HIV Web site](#).

Additionally, auditable outcome measures can be found in the [original guideline document](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on June 24, 2008. The information was verified by the guideline developer on October 20, 2008.

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